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APRIL 7, 1950



THE USE OF CLOUD CHAMBERS WITH
PULSED ACCELERATORS
EVANS HAYWARD

TECHNICAL PAPERS

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NEWS AND NOTES

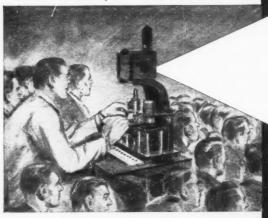


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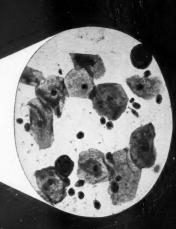
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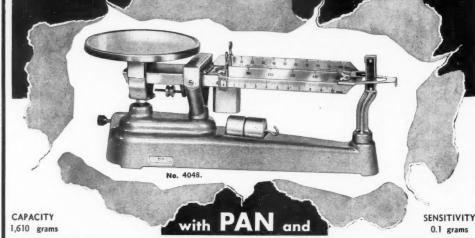
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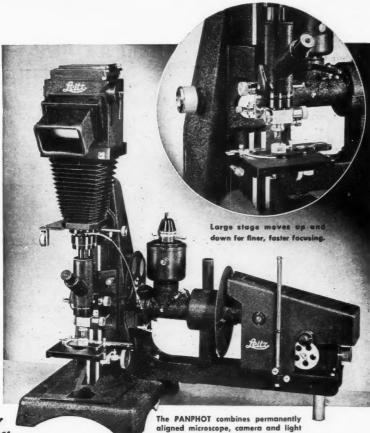
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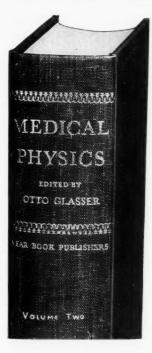
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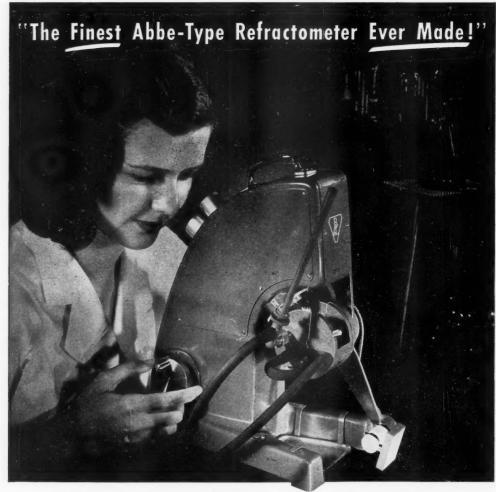
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The Use of Cloud Chambers with Pulsed Accelerators

Evans Hayward¹

Radiation Laboratory, University of California, Berkeley.

S LONG AS physicists have been studying charged particles, they have been developing new instruments to detect them or adapting the old ones to new circumstances. Although the Wilson cloud chamber (5, 7) is one of the oldest such devices, it is still being used extensively, especially in cosmic ray experiments and more recently in experiments in connection with high energy particle accelerators.

A cloud chamber is a machine that makes visible, and therefore enables one to photograph, the paths of charged particles: electrons, protons, mesons, etc. The chamber itself consists of a closed volume of gas saturated with a vapor. If the volume of the chamber is suddenly increased, droplets of the vapor will condense on the ions that any charged particle leaves behind as it passes through the gas. Immediately following the expansion, the chamber is illuminated by the flash of a very intense light and a camera then records the number and position of the drops, each one representing an ion produced during the flight of a charged particle and the whole group forming a trail that tells part of the particle's history.

The quantities that are most often measured with a cloud chamber are the ionization produced by a particle in going through the gas, its range, or its deflection by a magnetic field. The measurement of these quantities may serve simply to reveal the velocity, energy, or momentum of the particle or, if the identity of the particle is unknown, to determine its mass and charge.

As a charged particle traverses matter, it loses energy by ionization of the surrounding atoms, and as it does so, its velocity decreases so that it spends more time in any given region and hence produces more ion pairs per centimeter as it nears the end of its range. Since the energy loss varies with the density of the medium, a charged particle loses more energy per unit length of path in lead than in air. But for a given kind of particle (electrons excepted) moving in a given material, there is a unique relationship between

¹ I wish to thank Doctors Baldwin, Gaerttner, Koch, and Kruger for their courtesy in allowing me to include examples of their photographs. The previously unpublished pictures from Berkeley were taken by W. D. Hartsough, W. M. Powell, and the author under the auspices of the Atomic Energy Commission. its energy and both its range and its rate of energy loss by ionization. The ionization produced by a particle in traversing the gas of a cloud chamber may be measured by allowing the ions to diffuse before the expansion so that the droplets that condense on them are separated and can be counted. More often the density of a sharp track is observed and used as a qualitative indication of the ionization. The range of a low energy particle may be determined from the length of track it makes in the cloud chamber; the range of a more energetic particle may be obtained from the number and thickness of solid absorbers required to stop it.

Further, if a particle is moving in and perpendicular to the direction of a magnetic field, it experiences a force that is directed at right angles to the direction of both the field and the velocity of the particle. As a result the particle moves in a circle the radius of which is proportional to its momentum. Cloud chambers are therefore very often placed in magnetic fields so that curvature measurements may be made. It is desirable (although expensive) to have a magnetic field large in magnitude as well as extent, so that the deflection will be appreciable over a measurable length of track. In addition, it is necessary to make certain that the curvature of the track is produced by the force of the magnetic field on the particle and neither by the multiple scattering of the particle by the atoms of the gas nor by the distortion of the track by mechanical motions of the gas.

APPLICATION TO PULSED ACCELERATORS

In the last few years, cloud chambers have been used in connection with pulsed accelerators. It is the purpose of this paper to discuss some of the special techniques that may be applied under these circumstances and to point out their advantages (as well as their disadvantages) in comparison with cloud chamber techniques for, say, investigating cosmic rays.

To date, cloud chambers have been successfully operated in the x-ray beams from synchrotrons or betatrons and in the neutron beams from cyclotrons. An x-ray beam may be obtained from a betatron or synchrotron by allowing the circulating electron beam to strike an internal target. The electrons radiate and a beam is obtained which consists of quanta of all energies up to the energy of the electrons. Cyclotrons

usually accelerate either deuterons or protons and by allowing these particles to strike a target a beam of neutrons may be obtained. In either case, the resultant beam is one that does not directly produce many ions, but in its interaction with matter, secondary particles are produced which do ionize heavily. This is an ideal situation for a cloud chamber. If a cloud chamber is placed in an x-ray or neutron beam, several thousand quanta or neutrons may traverse the chamber but only those that interact with matter will be detected.

The most striking feature of using a cloud chamber with an accelerator is that the experimenter is able to control the time at which the pulse from the accelerator will arrive. If the curvature in a magnetic field is to be measured, the tracks should be distortionfree and as narrow as possible. It is, therefore, desirable to introduce the pulse at the end of the expansion after the gas stops moving but before thermal gradients between the gas and the chamber walls can produce convection currents. Distortions are thus minimized and the tracks are very sharp, since the ions do not have a chance to diffuse before the liquid is condensed on them. It should be pointed out that the opposite situation obtains in the most familiar type of cosmic ray experiment, where the cloud chamber is expanded by the pulse from a Geiger counter after the particle has gone through it. Any irregularities in the motion of the gas during the expansion are then superimposed on the track, and in addition the ions diffuse slightly between the time of passage of the particle and the time that they become laden with water.

The fact that the experimenter can control the time of arrival of the pulse is a great asset as far as the design of the magnet is concerned. The magnet does not have to be on all the time, but can be pulsed and synchronized with the cloud chamber cycle so that the field is at a maximum when the particles go through the chamber. This serves to minimize the heating of the magnet and as a result high currents may be used during the magnet pulse.

In ordinary cloud chamber operation an electric field is applied to remove ions between expansions and is then shorted out just before the fast expansion. Following the fast expansion the droplets fall toward the bottom of the chamber, although some of them evaporate en route. Those that exaporate remain floating around in the gas, since they are still too large to be removed by the clearing field; they would then be nuclei for condensation of vapor in the next expansion. Usually they are dissipated by one or more slow expansions, during which vapor is again condensed on them and they fall out. Slow expansions are extremely time-consuming, since after each expan-



Fig. 1.

sion the chamber gas must be allowed to come to the temperature of the walls. Gaerttner and Yeater (6) have very effectively eliminated the need for slow expansions. They "overcompress" the cloud chamber right after the photograph is taken; in this way the gas is heated up and the charged drops evaporate so that they are light enough for a strong clearing field to remove them. This technique has been developed to such an extent that photographs may be taken at the rate of one every five seconds. Since the usual time of a cloud chamber cycle is a minute or more, this development appears to be a real advance for those experiments that combine the use of a cloud chamber with an accelerator.

Illustrations. To illustrate the work that has been done to date, I have tried to collect examples of the different phenomena that have been observed with

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pulsed accelerators. The first eight pictures show events produced by neutrons (3, 4, 8, 11) and the last four, events produced by x-rays (1, 2, 9, 10). Each photograph represents events that follow a single pulse from the accelerator; each one shows the result of several hundreds or even thousands of traversals of the chamber by neutrons or photons.

Fig. 1-We want to study the events that result from the collisions that very energetic particles make with atomic nuclei. This photograph shows six nuclear disintegrations or stars produced when a single pulse of the 90-Mev neutrons (about 30,000 neutrons) from the Berkeley cyclotron traversed the cloud chamber. The chamber was filled with hydrogen and saturated with a mixture of alcohol and water vapor. Since the hydrogen nucleus consists merely of a single proton, its collision with a neutron would yield a single detectable fragment. The events in this picture must, therefore, represent the complete breakup of the carbon and oxygen nuclei present in the vapor. The most common isotopes of carbon and oxygen have nuclei consisting of equal numbers of protons and neutrons, six and eight respectively. Since a neutron bears no charge, it produces no ions and hence leaves no trace in a cloud chamber. This is unfortunate. It means that at least one fragment in most disintegrations is unaccounted for; since the observations are made on the charged components only, the interpretation is usually difficult and often impossible. In the photograph there are six stars, and starting from the top they have three, four, five, two, three, and four prongs. The first thing to notice is that the tracks are all bent into arcs of circles; this is, of course, the result of the force of a magnetic field on a moving charged particle. Since all of the particles are positively charged, they are curved in the same sense, clockwise. Notice how the heavier tracks steer a rather irregular course near the end of their range. Since they are moving rather slowly and are multiply charged, the collisions that they suffer with the nuclei of the gas are important enough to cause large deflections. Curvature measurements on these tracks are, therefore, not meaningful. The fine tracks are most certainly those of singly charged fragments and are probably protons. The fourth star is the most common type; it consists of one very fast proton track projected forward and a small blob of ionization produced by the recoiling nucleus. The last star at the bottom of the picture is made up of four doubly charged particles. In order to have eight charges in the first place, it must have been an oxygen nucleus and it is quite likely that all four fragments are alpha particles, since the alpha particle (two protons and two neutrons stuck together) is one of the more stable These stars are at least consistent configurations.

with the idea that the fast neutron strikes the nucleus, projecting forward one fast particle and leaving the nucleus excited so that in a very short time it explodes, sending lower energy particles in every direction. When a fast particle is not observed moving forward, it may mean that the fast particle is really a neutron, which makes no cloud chamber track.

Fig. 2 is taken from a study (4) of the fast par-

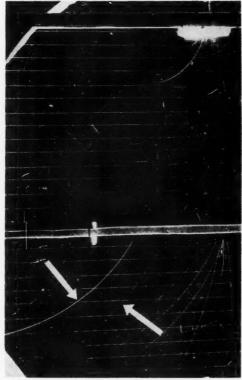


Fig. 2.

ticles that are projected forward when an energetic neutron strikes a nucleus. Instead of using the chamber gas as a target, the neutrons were allowed to strike a small piece of carbon placed within the cloud chamber. Many particles emanated from the target and some of them stayed in the plane of the cloud chamber long enough to pass through a glass absorber across a diameter of the chamber. The purpose of the absorber was to help in the identification of the particles; for a mere curvature measurement tells only the momentum, but if the curvature of a particle can be measured on two sides of an absorber of known thickness, then its mass may be determined at least well enough to identify the particle. The two tracks indicated by the arrows have almost the same radii as

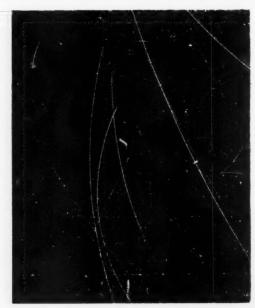


Fig. 3.

they leave the target, but on the far side of the absorber, one has a much smaller radius and an obvious increase in ionization. The other shows no apparent change in either. The first is a deuteron and the second, a proton.

Fig. 3 is a photograph from the data of an experiment (3) to determine the angular distribution of the protons that are scattered in elastic collisions with 90-Mev neutrons. Scattering experiments of this type give important information about the interactions between elementary particles. Here we see the tracks of six such protons that begin in the gas (H₂) after having been struck by an invisible but energetic neutron. The energy of the neutron may be obtained by applying the laws of elastic collisions and by simply measuring the curvature of the proton track and the angle it makes with the direction of the neutron beam.

Fig. 4 is from the data of a similar experiment (11) that used the 13-Mev neutrons from the Illinois cyclotron. Here the chamber was filled with CH₄ to 22 atmospheres, so that the knock-on protons would both start and stop in the gas. Since their energies could be obtained from their ranges, no magnetic field was necessary.

Mesons are the particles newest to nuclear physics. The term meson includes all the particles having masses between those of the electron and proton; we are now quite familiar with two kinds, π mesons and μ mesons. The π mesons have a mass of 276 electron

masses, bear both positive and negative charges, and interact very strongly with nuclei. They have attracted a great deal of interest because they are supposed to be responsible for the forces that hold nuclei together. A meson may be ejected in a collision in which there is available an amount of energy equivalent to its mass; it will be one of the fragments from a star produced by a very energetic particle. Fig. 5 is a photograph of just such an event. It was taken in the neutron beam that is produced when the 350-Mev protons of the Berkeley cyclotron strike a target. We have here a four-pronged star, the disintegration of an argon nucleus, in which one of the fragments is deflected by the magnetic field in the direction opposite to the others. It must therefore have a negative charge. This is believed to be an example of the



FIG. 4.

production of a negative π meson; its energy is 60 Mev. Though we cannot measure the ionization of this track, its density is certainly consistent with such an explanation.

When a positive π meson comes to rest, it decays into a μ meson (210 electron masses) plus some neutral particle. The μ meson that is produced always has an energy of 4 Mev and when it stops it decays into an electron and two neutrinos. The energy contained in the mass of the μ meson is divided between the rest

energies and kinetic energies of the three particles. The conservation laws impose the condition that the maximum energy available to the electron is 55 Mev, although it may have any energy smaller than this. Fig. 6 shows a π meson that enters an absorber and decays. It has been identified as a π meson because it has the appropriate curvature and ionization for one that could stop in the absorber; a μ meson of the same curvature would get through. The μ meson, which is its decay product, also stops in the absorber and the track of the electron that results from its decay is the small, faint circle in the corner of the cloud chamber.



Fig. 5.

When a negative π meson stops in matter, it is captured by a nucleus; the nucleus is thus supplied with some extra energy which causes it to break up. Fig. 7 shows the track of a negative π meson, which shows a decrease in radius of curvature as its ionization increases until it finally stops and is captured by an argon nucleus. This star consists of a single prong produced by the recoiling nucleus; presumably neutrons are emitted as well.

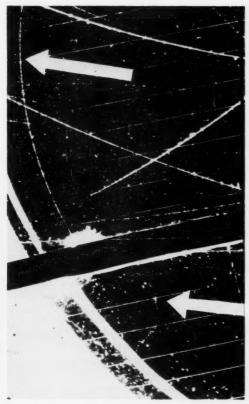


Fig. 6.



Fig. 7.

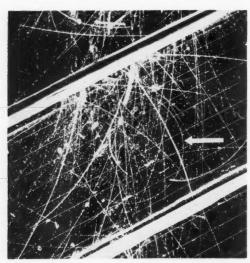


Fig. 8

Fig. 8 is included to demonstrate how a low energy meson may be identified from its curvature and ionization against a rather high background of heavy nuclear fragments. It shows a density of ionization much greater than that of an electron and yet it cannot be a proton because protons always stop before they can

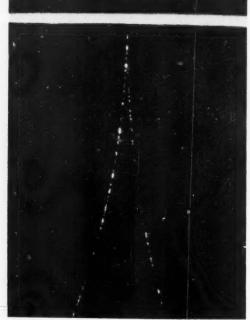


Fig. 9.

be wound up into such small circles. It is a meson, but it would be impossible to say whether it is a π or a μ .

It is important to study how mesons are made, the characteristics of their decay, and how they interact with various nuclei. Physicists are hard at work trying to make observations on them. Figs. 5, 6, and 7 are the best cloud chamber pictures of artificial mesons that have been taken to date and Fig. 8 shows why there aren't any more.

The beams of photons from betatrons and synchrotrons are produced when the circulating electron beam strikes an internal target. The electrons are decelerated in the fields of the nuclei of the target material, and as a result, photons are emitted; these photons may have any energy up to the full energy of the incident electron. The beam thus consists of a continuous spectrum of x-ray energies.

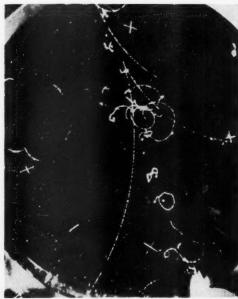


Fig. 10.

Now if a photon has energy greater than about one million electron volts (Mev), it is capable of producing an electron-positron pair when it passes near a nucleus. Approximately one Mev is used up in producing the pair, and the remaining energy goes into the kinetic energy of the positron and electron. Fig. 9 shows an example of pair production. This photograph was taken of the aforementioned "overcompression" chamber in the x-ray beam from the 100-Mev betatron at the General Electric Research Laboratory. The materializer is a lead plate oriented perpendicular to the beam direction. The electron and positron

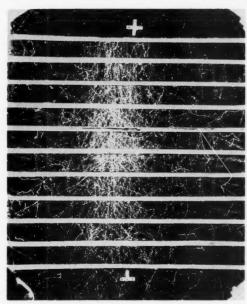


Fig. 11.

curve away from each other in the magnetic field. The energy of the incident photon has been determined from their radii of curvature to be 25 Mev. Fig. 10 is a similar photograph taken in an experiment (10) to determine the energy spectrum of the photons from the 20-Mev betatron at the University of Illinois. The pair represented here was produced in the gas, in the field of an argon nucleus. The low energy electrons do not bend into smooth curves because they are scattered rather badly by the gas.

If the electron or positron continues through a medium of heavy nuclei, it will radiate quanta and these quanta will make more pairs and so on until the average energy of the electrons and photons is so low that they cannot radiate and produce pairs as efficiently as they can lose energy by other means. Then the electrons are absorbed by ionization and the photons by their collisions with electrons which are in turn absorbed by ionization.

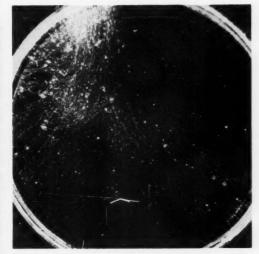


Fig. 12.

The best way to observe this so-called shower is to place a series of lead plates in a cloud chamber in the x-ray beam. See Fig. 11. This cloud chamber was in the beam that is produced when the 335-Mev electrons of the Berkeley synchrotron strike an internal target. The shower is due to the several hundred photons that are contained in a single pulse from the synchrotron. The photograph shows how the number of electrons increases rapidly with thickness up to a maximum under the fourth lead plate (they are each $\frac{1}{8}$ inch thick) and after that the number decreases slowly as the lower energy electrons are absorbed. Notice how the low energy electrons scatter in the gas (argon).

Fig. 12 (2) shows a star produced by a photon from the 100-Mev betatron. It is analogous to those made by high energy neutrons but a much rarer event. This particular star is probably the disintegration of a nitrogen nucleus, since the chamber was filled with air. Notice the large numbers of electrons and positrons that make up the background; their presence is sufficient to show that a photon is much more likely to make a pair than a nuclear disintegration.

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Technical Papers

Cyanide Protection against X-Irradiation

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The recent report of Patt et al. in Science (15), showing a cysteine protection against x-irradiation, increases the interest of our observations on a similar protection by cyanide, reported March 26, 1949 at the Société Belge de Biologie (5 and 6).

Recent papers by French and English physical chemists showing the presence of hydrogen peroxide in irradiated water suggested experiments on frog's isolated rectus abdominis (7, 14). This muscle, irradiated with therapeutic doses of x-rays or dipped in a solution containing P₁₅²⁸ in form of phosphate, showed when stimulated with KCl a contracture very similar to that observed by Bacq (1, 2) after the action of H₂O₅.

Dustin and Gompel (10) injected hydrogen peroxide intraperitoneally in mice and showed that it was a radio-mimetic poison. These observations were in agreement with our general ideas on the actions of oxidizing agents as "thioloprive" substances (3, 4). Frederic (12) has shown that the —SH groups disappear in the skin of the guinea pig after x-ray irradiation.

Two of us (13) succeeded with the semicarbazone of adrenochrome (Adrénoxyl Labaz), which increases capillary resistance in inhibiting the x-ray purpura in mice; but this substance does not change the mortality. Field and Rekers (11) with flavonids possessing vitamin P action, succeeded in decreasing x-ray mortality.

Striking results have been obtained with sodium (or potassium) cyanide. Our technique was as follows. Mice of pure breed (C 57 black or A.K.A.), weighing about 30 g and 4 to 6 months old, were irradiated by groups of 10, using 230 kv, 12 ma, copper filter 0.25 mm, focal distance 50 cm, field 100 cm2, mean output 30 r per min. The 42 control mice receiving 500 r to 600 r all died between the 4th and the 8th or 9th day. Animals receiving 0.1 mg NaCN just before similar irradiation showed 50% to 80% survival. The same dose of NaCN given immediately after irradiation only delayed mortality. When the cyanide was injected 15 min after irradiation, the mortality curve was exactly the same as that of the controls (Fig. 1). A statistical analysis does not seem necessary to show that these results are highly significant. Our conclusions are based on the observation of 11 groups of 10 mice each. Cyanide is rapidly detoxicated in -SCN by an enzymatic system localized in the liver, but NaSCN either has no effect or shortens the survival period of irradiated mice. Thus it is the CN- anion that is responsible for this protective action. We have not yet collected the various facts that would allow us to give a reasonable interpretation of this action of cyanide, but several possibilities may be discussed in the light of the similar

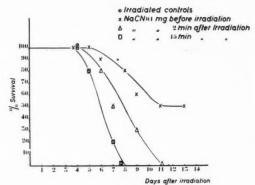


Fig. 1.

successful experience of Patt et al. with cysteine.

Cyanide reduces disulfide bonds (—S—S—) to sulfhydryl groups —SH. We do not believe, however, that the dose of cyanide injected is sufficient to give an effective reducing concentration; maximal tolerated amount of BAL (1.7 mg) injected in mice before irradiation only delays mortality; there is no permanent survival. One may suspect that the interpretation of the results of Patt et al. is not as simple as it seems at first sight, because preliminary experiments have shown in our laboratory that the level of reduced glutathione in blood and tissues (liver, kidney, heart, and muscle) of mice is not lowered after lethal irradiation. The failure of cyanide or cysteine to act when given after irradiation shows that the biochemical lesion in vivo is not as easily reversible as —SH enzyme inactivation in vitro (8, 9).

Cyanide might simply reduce temporarily the metabolic activity of the animal. It is known that there is a certain parallelism between total metabolism and radiosensitivity: an increase of metabolism is associated with increased sensitivity, whereas relative resistance is observed with anoxic tissues.

Cyanide might also inhibit some heavy metal enzyme responsible for the rapid disposal of $\mathrm{H}_2\mathrm{O}_2$, thus decreasing the rate of reaction of this peroxide with some reducing substance in the tissues. Experiments are in progress to test these various possible interpretations.

Thus, we may conclude that cyanide, but not thiocyanate, protects a significant percentage of mice irradiated by a lethal dose of x-rays, that this poison is ineffective when given after irradiation, and that many more experiments are needed in order to be able to give a correct interpretation of these facts.

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Serological Relationships between Nucleus, Cytoplasm, and Cytoplasmic Products and the Concept of Complementary Molecules

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The concept of antibodies as units complementary to their antigens was originated by Breinl and Haurowitz (2). Pauling (10) has developed the idea of antibody specificity as resulting from the folding of initially stretched-out polypeptide chains over limited regions of the antigen. The molecules thus folded into specific configurations become stabilized by bonds acting between their folds, and thereafter "fit" the specific regions of the antigen. Such complementary molecules (antibodies) can subsequently combine with their antigens, since the configurations permit the very close juxtaposition of combining groups necessary for bonding. The hypothesis does not neglect the role of chemical composition in specificity, for the nature and arrangement of the residues will determine the type of folding possible at various points along the polypeptide chain. Nevertheless, chemical composition provides only the potentialities for specificity or a limited degree of specificity, the maximal degree being achieved by the folding process.

The possibility of applying the concept of complementariness to the more general problem of specificity in biological synthesis has been broached in several recent discussions (4, 11, 13). As Tyler (12, p. 13) has stated,

Any of the macromolecular constituents synthesized in a cell would be complementary to the substances comprising the sites of synthesis. Since growth consists primarily in the formation of such substances that comprise the integral structure of the cell, we may regard the mechanism of the process of growth to be essentially analogous to that manifested in antibody formation.

The liver offers favorable material for the testing of this hypothesis, since the three broad elements in the chain of synthesis (nucleus, cytoplasm, cytoplasmic products) are readily available. If (1) nuclear constituents are the prime determiners of cytoplasmic activity, as ample evidence from classical and biochemical genetics

would indicate, and (2) the cytoplasm is in turn a site of synthesis, then we might expect the complementary relationships diagramed in Fig. 1. Nuclear constituents (perhaps highly polymerized nucleohistones) serve as templates (N1) for the synthesis of complementary cytoplasmic constituents, some of which act as templates (C1) for the synthesis of cytoplasmic products (P1), which in the present instance would be the serum proteins of hepatic origin. Omitting from consideration many obvious complicating factors (intermediate products, metabolic modifications, etc.), we should expect the serum products to have configurations resembling, although not perhaps exactly duplicating, the original nuclear templates. Furthermore, if antibodies contain configurations complementary to limited regions of the antigens, we may expect the general antibody-antigen relationships shown in Fig. 1. As indicated by the arrows, antinuclear bodies should react maximally with nuclear material and serum, while antiserum bodies should react maximally with nuclear and serum constituents. This is not what would be predicted on the basis of chemical composition; cytoplasm and serum certainly show a greater over-all chemical resemblance to one another than do nucleus and serum.

Rat liver nuclei and cytoplasm were separated by the Dounce method (3), using M/475 citric acid in the first step and distilled water at pH 5-7 thereafter. The injection of whole nuclei into rabbits indicated a low degree

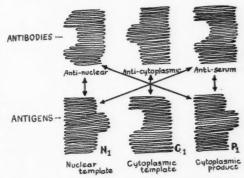


Fig. 1. Schema showing postulated complementary configurations of macromolecules of nucleus (N1), cytoplasm (C₁), and cytoplasmic products (P₁). Portions of molecular chain represented by coiled lines. The arrows indicate expected maximal cross reactions between antibodies and an-

of antigenicity; hence the nuclei were treated with 10% NaCl solution to extract the nucleohistone (9) and make it available to the antibody-forming mechanism. All steps in the isolation and extraction procedures were carried out in the cold (6° C or below). The whole nuclei in 10% NaCl, alone or mixed with swine serum as adjuvant, were dialyzed first against water and then against physiological saline to remove excess salt and recombine the nucleic acid and histone. The products were injected intramuscularly and intraperitoneally into New Hampshire and White Leghorn fowl, and showed clear antigenicity. The following antigens were each injected into two birds, which were bled 8 days after the last injection:

- (A) Nuclei treated as described, with 10% NaCl and dialysis.
- (B) Nuclei treated as in (A) and mixed with swine serum as adjuvant.
- (C) Defatted nuclei (using cold alcohol-ether, 1:1) suspended in 0.9% saline.
 - (D) Rat serum.
 - (E) Liver cytoplasm in 0.9% saline.
- (\mathbf{F}) Liver cytoplasmic fraction insoluble in 0.9% saline but soluble in 10% saline.

Antisera against these antigens were tested by layer-

TABLE 1

CROSS REACTIONS OF ANTINUCLEAR AND ANTICYTOPLASMIC ANTIGENS AND ANTISERA*

	Antisera versus :						
Test antigens† mg/ml‡	(A) Nuclei	(B) Nuclei + swine serum	(C) Defatted nuclei	(D) Rat serum	(E) Whole cytoplasm	(F) 0.9% Insoluble cytoplasm	
A ₁ Nuclear extract							
3.0 mg	100	40,000	10	10	100	10	
C1 Defatted nu-							
clear extract	undi-						
14.6 mg	luted	10	10	20,000	10	0	
D ₁ Rat serum§	1000	40,000	0	40,000	0	0	
EF1 Cytoplasm							
23.5 mg	10	1000	100	10	100	100	

TABLE 2

ABSORPTION OF ANTINUCLEAR SERA WITH CYTOPLASM
AND RAT SERUM*

		Inabsorb antisera	Absorbed antisera			
Test antigens† mg/ml‡	(A) Nuclei	(B) Nuclei + swine serum	(C) Defatted nuclei	(A) Nuclei	(B) Nuclei + swine serum	(C) Defatted nuclei
A: Nuclear extract	100	1000	10	1000	1000	10
C ₁ Defatted nu- clear extract	1000	1000	1000	1000	1000	1000
D ₁ Rat serum§	1000	40,000	0	0	0	0
EF1 Cytoplasm#	10	1000	100	0	0	0

Note: Footnotes are applicable to all four tables. Controls, not given in tables, were normal fowl serum layered against test antigens and antisera layered against 10% saline.

- * Titers given as reciprocals. † Fraction soluble in 10% saline.
- ‡ Solids in mg/ml of undiluted antigen; values given in Table 1 apply to corresponding test antigens in all tables.
- § Rat serum diluted 1:1 with 20% NaCl solution.
- || Pooled cytoplasm from second and subsequent steps of Dounce's method.
- ¶Unabsorbed antisera diluted with 10% saline to correspond to dilution of absorbed antisera, except in Table 4,

ing against dilutions of the following test antigens:

- (A1) Nuclear fraction soluble in 10% saline.
- (C_1) The 10% saline-soluble fraction from defatted nuclei.

(EF₁) Cytoplasmic fraction soluble in 10% saline. The antisera were diluted 1:1 with 20% NaCl solution, since the test antigen dilutions were prepared with 10% NaCl.

Table 1 shows the cross reactions obtained. Antinuclear sera reacted with all the test antigens, giving titers which conform on the whole with expectations derived from the concept of complementariness as here applied. Despite the low concentration of the nuclear test antigen (3.0)

TABLE 3

Absorption of Anticytoplasmic Sera with 10% Soluble Nuclear Extracts*

			Antisera absorbed with :				
Test antigens† mg/ml;		osorbed isera¶	Nuclei, 10% NaCl fraction		Defatted nuclei 10% NaCl fraction		
	(E) Whole cytoplasm	(F) 0.9% Insoluble cyroplasm	(E) Whole cytoplasm (E) Whole	cytoplasm	(F) 0.9% Insoluble cytoplasm	(F) 0.9% Insoluble extoplasm	
A ₁ Nuclear extract	100	10	0	0	0	0	
C ₁ Defatted nu- clear extract	10	0	0	0	0	0	
D ₁ Rat serum§ EF ₁ Cytoplasm	0 100	100	100	100	0 100	100	

TABLE 4
ABSORPTION OF ANTISERA WITH CHICKEN RED BLOOD CELLS*

	Antisera versus :						
Test antigens† mg/ml‡	(A) Nuclei	(B) Nuclei + swine serum	(C) Defatted nuclei	(D) Rat serum	(E) Whole eytoplasm	(F) 0.9% Insoluble cytoplasm	
		Unal	bsorbe	antise	era¶		
A ₁ Nuclear extract	100	100	1000	10	100	10	
C ₁ Defatted nu-							
clear extract	100	100	100	100	10	undil.	
Hemolysis**	+	+	?	+	+	+	
	A	ntisera a	absorb	ed with	red ce	ells	
A ₁ Nuclear							
extract	100	100	10	100	100	10	
C ₁ Defatted							
nuclear extract	100	100††	100	100	10	10	
Hemolysis**	0	0	0	0	0	0	

in which 0.9% saline was used for dilution in hemolysis experiments: thereafter the salt concentration was increased to 10% for the test antigens.

** Suspensions of red blood cells tested: 0.2, 0.33, 0.5, 1.0, and 2.0%.

†† Titer possibly higher, since this was highest dilution tested.

mg/ml) and the high concentration of cytoplasmic antigen (23.5 mg/ml), the titer for the latter was low. The presence of swine serum (which probably formed conjugates with dissociated nucleic acid [5]), increased the titers generally but did not change the basic relationships.

Extracts of defatted nuclei gave titers similar to those obtained with whole nuclei except in the case of serum for which titers were low or completely negative. This, together with the titers shown by most of the antisera for defatted nuclear extracts, suggests that nuclear lipids are antigenically active. The situation is, however, by no means clear-cut, since antiserum (D) reacted to unusually high titer with defatted nuclear extract. Strict comparison between antisera (A) and (C) is not warranted, since the defatted nuclei were not treated with 10% saline.

Antirat serum showed highest titers with defatted nuclei (C1) and serum (D1). The low titer with whole nuclear extract does not conform to expectations unless we consider the low concentration of this test antigen.

Anticytoplasmic sera (E, F) showed little or no activity for serum (D1) but gave unexpected high titers with nuclear extract (A1). These results suggest a high degree of resemblance between nuclear and cytoplasmic constituents; in fact, the titers were as high as those obtained with antinuclear sera (A), and recall the numerous observations indicating the passage of nuclear constituents into the cytoplasm (cf. 8).

On the basis of complementariness (as well as the general chemical and enzymatic differences between nucleus and cytoplasm), we might expect antigenic specificity for both nucleus and cytoplasm. The results of absorption experiments are shown in Tables 2 and 3. Antinuclear sera absorbed with serum and cytoplasm retain essentially the same titers for nuclear extracts (Table 2). Anticytoplasmic sera absorbed with either whole nuclear or defatted nuclear extract also retain their anticytoplasmic activity (Table 3). Serum apparently also shows antigenic specificity distinct from that of the nucleus and cytoplasm, since anticytoplasm reacts very poorly or not at all with serum. However, this point was not tested directly. We should expect to find antiserum bodies which are nonreactive with liver cell constituents, since serum constituents are not exclusively of hepatic origin (e.g., pituitary factors, gonadal hormones, etc.).

Nuclear, cytoplasmic, and serum specificity were further demonstrated by absorption with chicken red blood cells (Table 4). The antisera showed hemolytic activity shortly after they were obtained. The hemolytic activity was lost after storage for seven weeks in the cold and was not renewable by the addition of fresh guinea pig serum. Although this indicated the absence of hemolysins, the antisera were absorbed with a 4% suspension of fowl red blood cells. As shown in Table 4, the titers for nuclei, cytoplasm, and serum were little affected, with the exception of the antidefatted nuclear serum (C).

We believe that nuclear specificity may have a significant bearing on theories of embryonic differentiation. If one could obtain all the products synthesized by liver cytoplasm, then on the basis of complementariness the cell products (P1 in Fig. 1) should be able to combine with all antinuclear bodies. Our closest approach to an experiment like this was the absorption of antinuclear sera with both liver cytoplasm and serum (Table 2). This presumably provides all the products synthesized by liver cytoplasm, whether they retain an intracellular position or are extruded into the serum, with the possible exception of fibrinogen and other proteins possibly removed with the blood clot. The fact that such absorption left antibody activity specific for the nucleus suggests that some constituents of the liver nucleus are not concerned in synthesis. From the point of view of cellular differentiation it will be of interest to ascertain whether such nucleus-specific antibodies also occur in nuclei from other tissue, and if so whether or not they are identical.

Earlier work on the antigenicity of nuclear constituents (reviewed in 6, 14) was based on extracts of whole tissues rather than on isolated nuclei, and in all probability involved higher degrees of denaturation and degradation than is produced by more recent methods. The results were conflicting both as to the antigenicity and specificity of nuclear constituents. The more recent work of Maculla (7) was also done on extracts of whole tissues, but some of her results (particularly on liver fractions) are in good agreement with corresponding portions of our data. Results with other organs (e.g., lung and kidney) did not accord with those for liver. Arnesen et al. (1) did not find evidence of specificity as between nuclei and various cytoplasmic granules of the spleen. However, they utilized the complement fixation method and whole nuclei, which made only the nuclear surface available for antibody combination.

Perhaps the essential phenomena brought out by the present study are: (1) on the basis of antibody titers certain constituents of serum have a greater resemblance to certain nuclear constituents than to cytoplasmic constituents; (2) similarly, nuclear constituents of the liver resemble serum more than they do liver cytoplasm; and (3) the nucleus and cytoplasm contain constituents (or determinants) distinct from one another, and from those in serum and on the surface of red blood cells of the same species.

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Pyrolysis of Hydrocarbon Polymers

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In some recent work at the National Bureau of Standards, pyrolysis was carried out in a vacuum of about 10^{-6} mm Hg, and at temperatures ranging between 350° and 450° C, on polystyrene (1), polyisobutene, polyisoprene, polybutadiene, GR-S (25% styrene), and polyethylene (2). A sample of the polymer weighing about 50 mg was spread as a layer about 40 μ thick on a platinum tray and pyrolyzed in an evacuated Dewar-like apparatus by means of a platinum wire resistance furnace placed inside the apparatus. The products of pyrolysis were fractionated to facilitate analysis of composition by the mass spectrometer, or determination of the average molecular weight by a micromethod involving lowering of the freezing-point. The following fractions were obtained:

I. A solid residue, difficultly soluble in benzene or cyclohexane. No analysis was made of the composition or average molecular weight of this fraction, except in the case of polystyrene, where the average molecular weight was found to be of the order of 2000-2500.

II. A waxlike fraction volatile at the temperature of pyrolysis, but not volatile at room temperature. This fraction was quite soluble in benzene or cyclohexane and its average molecular weight was determined. No mass spectrometer analysis was made of this fraction.

IIIB. A liquid fraction volatile at room temperature but not volatile at -75° C. No mass spectrometer analysis or molecular weight determination was made of this fraction. Its average molecular weight was estimated to be about 150 in all cases.

IIIA. A liquid fraction volatile at -75° C. Mass spectrometer analysis of this fraction showed it to consist of the monomer and other compounds of a molecular weight less than that of the monomer or dimer. The average molecular weight could be calculated in this case from the data obtained in the mass spectrometer analysis.

IV. A gaseous fraction volatile at -196°C. This fraction was analyzed in the mass spectrometer and was found to consist in all cases of CH₄.

Within the temperature range specified, the relative amounts of the volatilized fractions and their average

molecular weights for any polymer were found to be fairly constant, independent of temperature or extent of pyrolysis. The various fractions and their average molecular weights are shown in Table 1 for five polymers and one copolymer, GR-S. The data in this table can be used to calculate the number of ruptures of carbon to carbon links occurring in the macromolecular chain due to pyrolysis. In this calculation it is assumed that the polymer consists of one very long chain, and a double bond is counted like an ordinary C-C link.

Let Y_f be the yield of any given fraction in weight percent of the total volatilized part and M_f the average molecular weight of this fraction. Then the total number of molecules, small or large, which is the same as the total number of ruptures, P, per 100 g of a given polymer, is given by the expression

$$P = N \sum \frac{Y_f}{M_f}$$

where N is the Avogadro number.

The total number P_0 of C-C links in the macromolecular chain in 100 g of any polymer can be obtained by dividing the weight of the polymer by the average molecular weight per carbon in the chain and multiplying by N. Thus, for example, in the case of polystyrene

the average molecular weight per carbon in the chain is 104/2 = 52, and the number of C-C links in 100 g is

$$P_0 = \frac{100 \times N}{52} = 1.923N$$

Ratio R of ruptured links P to original links P_0 can then be expressed in percent. Thus,

$$R = \frac{P \times 100}{P_0}$$

Table 2 shows values of P, P_0 , and R for five polymers and one copolymer.

In the pyrolysis of hydrocarbons of ordinary molecular

TABLE

FRACTIONS OBTAINED IN THE PYROLYSIS OF SOME HYDROCARBON POLYMERS AND THEIR AVERAGE MOLECULAR WEIGHTS

Delemen	Waxlike II		Liquid IIIB		Liquid IIIA		Gas IV	
Polymer -	% *	mol. wt	% €	mol. wt	% *	mol. wt	% *	mol. wt
Polystyrene	57.8	264			42.1	103.2†	.10	16
Polyisobutene	68.3	543	9.5	150	22.0	57.1	.22	16
Polyisoprene	88.7	577	5.6	150	5.7	68.5	.02	16
Polybutadiene	85.7	739	9.8	150	4.2	51.0	.30	16
GR-S	88.0	712	7.9	150	3.9	47.9	.19	16
Polyethylene	96.6	692	2.3	150	1.1	53.1	trace	16

* Percent of the total volatilized part.

† In the case of polystyrene, the fraction classed under IIIA was collected at room temperature. Mass spectrometer analysis showed it to consist of 95 mole % styrene and 5 mole % toluene. There was no IIIB fraction from this polymer.

TABLE 2
PERCENT OF RUPTURED C-C LINKS IN THE
TOTAL PYROLYZED PART*

Polymer	Original No. of links Po	No. of ruptured links P	$R = \frac{P \times 100}{P_{u}}$
Polystyrene	1.923N†	.634N	33.0
Poly'sobutene	3.572N	.588N	16.5
Polyisoprene	5.882N	.276N	4.7
Polybutadiene	7.407N	.283N	3.8
GR-S	6.061N	.270N	4.5
Polyethylene	7.143N	.175N	2.5

* Calculated for 100 g of the polymer.

 $\dagger N = Avogadro's number.$

size, decomposition does not take place until a temperature of about 800° C is reached. However, the introduction of a small amount of free radicals into the system induces the rupture of C-C links to take place at temperatures as low as 300° C (3). Since the hydrocarbon polymers discussed here decompose on heating at temperatures of 350°-450° C, it can be assumed that here too decomposition is due to the presence of free radicals.

TABLE 3

DISTRIBUTION OF C-C LINK RUPTURES BETWEEN SMALL AND LARGE MOLECULES*

D-1	Monome molec		Intermediate and large molecules		
Polymer	Fraction IIIA	Fraction IV	Fraction IIIB	Fraction II	
	%	%	%	%	
Polystyrene	64.6	0.8		34.6	
Polyisobutene	visobutene 65.4		10.7	21.5	
Polyisoprene	30.1	0.5	13.4	56.0	
Polybutadiene	29.1	6.7	23.0	41.2	
GR-S	30.1	4.5	19.7	45.7	
Polyethylene	11.9	8.5		79.6	

* Calculated in percent of total number of ruptures.

It is also assumed that the free radicals are the ends of the macromolecules, where rupture of C-C links to give molecules of monomer size may start. These free end radicals may in addition cause rupture of C-C links at some other points throughout the chain whenever they come up against these points at random.

Three mechanisms of chain rupture can be visualized:

1. Small fragments of monomeric size break away at the ends of a macromolecular chain until the residual fragment is small enough to escape into the gaseous phase at the temperature of pyrolysis. The products of pyrolysis will consist mainly of small-sized molecules.

2. The macromolecule breaks at random until fragments are sufficiently small to vaporize. In this mechanism the larger molecules, above the monomeric size, will predominate in the vaporized product.

3. A combination of mechanisms 1 and 2 giving rise to a mixture of small and large molecules, the ratio of the two groups of fragments depending on the polymer.

Table 3 shows the relative number of C-C ruptures due

to monomeric type molecules (fractions IIIA and IV) as compared with the number of ruptures due to medium- and large-sized molecules (fractions IIIB and II), on the basis of $R=R_1=100$. It can be seen from this table that mechanism 1 predominates in the case of polystyrene and polyisobutene; mechanism 2 predominates in the case of polyethylene; and mechanism 3 in the case of the other polymers.

Some experiments carried out in this laboratory on the pyrolysis of polymethylmethacrylate at 400° C showed that about 90% of the C-C link ruptures were due to the formation of the monomer. This, then, represents a case where ruptures of C-C links occur almost exclusively at the ends of the macromolecular chains.

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Di-(p-chlorophenyl)methylcarbinol, a New Miticide¹

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In the course of a research program on synthetic organic insecticides related to 1,1-di-(p-chlorophenyl)-2,2,2-trichloroethane (DDT), the di-(p-halophenyl)alkylearbinols (p-XC₀H₄)₂C(OH)R, showed high initial and residual toxicity to mites (5). This paper is a preliminary report on certain properties of this class of compounds.

Miticides have become indispensable since the widespread use of DDT. DDT is not only ineffective against this class of agricultural pests, but it also promotes the growth of mites by destroying predatory insects.

The di-(p-halophenyl) alkylcarbinols are unusual in the high specificity of their action. Although tests have been run against a wide variety of insects, only mites are affected at practical levels of concentration. Red spiders, European red mites, two-spotted mites, and Pacific mites can be controlled. There is no plant damage under ordinary spraying conditions. The mode of action has not been definitely established, but these compounds appear to be contact poisons.

Although exhaustive toxicity tests on laboratory animals have not been run, preliminary results with the di-(p-chlorophenyl)methylcarbinol on rats indicate acute and chronic toxicities which are not greater than DDT (4) and which subsequent study may show to be even lower. In the manufacture of pilot plant batches on a

¹ U. S. Patent 2,430,586, November 11, 1947, R. F. Ruthruff, Oliver Grummitt, and B. C. Dickinson, assigned to the Sherwin-Williams Company, Cleveland, Ohio.

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tonnage scale, no harmful effects have been observed on plant personnel exposed over several months.

The most important member of the class, because of its accessibility and cost, is di-(p-chlorophenyl) methylcarbinol, $(p\text{-ClC}_0H_*)_2\text{C}(\text{OH})\text{CH}_3$, which was first made by Bergmann and Bondi in 1931 by the action of methylmagnesium iodide on p,p'-dichlorobenzophenone $(1,\beta)$. It can also be made by other Grignard reactions such as the action of p-chlorophenylmagnesium bromide on ethyl acetate or on p-chloroacetophenone. The p,p'-dichlorobenzophenone, not available commercially, can be made by several Friedel-Crafts reactions, including chlorobenzene with carbon tetrachloride, with phosgene and, with p-chlorobenzopl chloride. Oxidation of DDT ethyene, 1,1-di-(p-chlorophenyl)-2,2-dichloroethylene, yields this ketone, a reaction which first showed the structure of DDT (2).

Di-(p-chlorophenyl) methylcarbinol is a colorless, crystalline solid, melting at 69.5°-70.0° C. It cannot be vacuum-distilled at 1-mm pressure or vacuum-sublimed without decomposition. Thin films exposed to air at room temperature for 42 days volatilized less than 2%. It is insoluble in water, soluble in the common organic solvents, and most soluble in the polar type such as alcohols, ketones, etc. As a tertiary alcohol, this compound may be dehydrated to 1,1-di-(p-chlorophenyl) ethylene, mp 84°-86° C, by the prolonged action of heat above its melting point or by the catalytic action of strong acids in solution. Oxidation of the carbinol yields p,p'-dichlorobenzophenone. Catalytic reduction yields 1,1-di-(p-chlorophenyl) ethane. Typical alcohol derivatives such as ethers and esters are difficult to prepare because of the ease of dehydration and the sterically hindered alcohol group.

Various analytical procedures for the carbinol and related compounds have been developed. Traces of the carbinol may be estimated colorimetrically by nitration followed by treatment with alkali. The carbinol and its isomers are analyzed by measuring the water of dehydration either by Karl Fischer titration or volumetrically, if large samples are taken. Quantitative oxidation of a mixture containing carbinols and the corresponding ethylenes and ketones in which the chlorine atoms are in the p,p' and o,p' positions of the rings gives a mixture of p,p' and o,p'-dichlorobenzophenones whose composition can be estimated from setting point-composition data. From water yield and oxidation results, concentration of the most active isomer, di-(p-chlorophenyl)-methylcarbinol, can be calculated. Ultraviolet absorption spectra and setting point-composition diagrams are also useful in analyzing mixtures of carbinol, ethylene, and ketone.

From the preparation and testing of a number of derivatives and analogues of the di-(p-halophenyl) alkyl-carbinols, certain conclusions on the relation of structure to activity may be drawn. For maximum activity the ring halogen atoms are necessary. Isomeric carbinols with one or both of the halogens in the ortho position are much less active. The alkyl group, R in $(p\text{-ClC}_0H_4)_2\text{C}(OH)R$, may be methyl, ethyl, etc., or cycloalkyl such as cyclohexyl, but aryl or aralkyl groups such as phenyl and benzyl give com-

pounds of lower activity. If the alcoholic group is shifted from the tertiary carbon atom, as in the isomeric B-β-di-(p-chlorophenyl) ethanol, the miticidal activity is lost.

The details of these properties, syntheses, and analyses will be published at a later date.

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Localization of C¹⁴ in the Tissues of Mice after Administration of C¹⁴ Methyl-labeled Glycine¹

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Carbon-labeled compounds offer a wide range of experimental possibilities because of the ubiquity of carbon in living organisms. Because of its long half-life, C¹⁴ offers the additional advantage of an isotope that can be studied over long periods of time. However, this very fact has resulted in an understandable hesitation to use it, without more knowledge regarding the effects of prolonged exposure of living tissues to radiation. It was felt that if the radioactivity were fairly evenly distributed in the organism, the total dose could be so calculated as to keep the radiation to any one tissue or organ within a reasonably calculated safety margin.

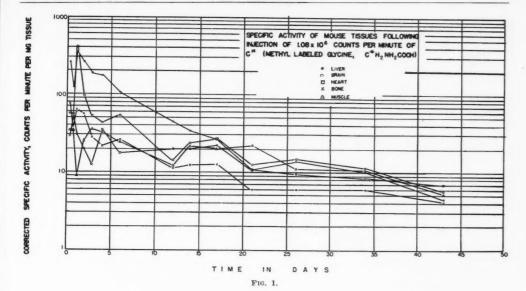
Bloom et al. (1), using BaC*O₃ or NaHC*O₃ injected intraperitoneally into young rats, showed by means of autoradiographs that activity tended to localize in bone and remain there long after soft tissues were no longer active, although the activity in various tissues was not directly weighed and measured, so that the residual activity in bone may have been extremely small. It was felt, therefore, that further work should be done to see if use of soluble compounds resulted in radioactivity localizing in the bone.

Glycine, labeled with C^{14} in the methylene position, having an activity of 567,000 cpm (4.57 c/mg) prepared by Ostwald (3) was injected into the tail veins of adult, male, strain A mice. Each animal was injected with 1.728 mg of glycine*, a total activity of 1.08×10^6 cpm. Fifteen animals were injected simultaneously and sacrificed at varying time intervals from 6 hr to 43 days. Some were sealed in glass metabolic eages so that activity measurements of breath, feees, and urine could be made. Combustions, plating, corrections, etc. were carried out as described by Calvin et al. (2). The moisture removed by vacuum desiccation (in order to obtain dry tissues)

⁵ Sometimes abbreviated to DMC. Spraying compositions containing DMC have the trade-marked name of Dimite.

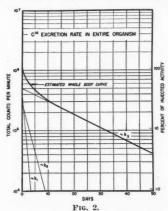
¹The work described in this paper was sponsored by the Atomic Energy Commission.

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was collected in a liquid nitrogen trap and subjected to wet combustion (4) to determine the presence of any volatile activity in two cases. Less than $\frac{1}{2}$ cpm was present in the entire sample, so it was felt reasonable to ignore this as a possible site of activity loss. Reid (5), using DL-tyrosine labeled with C¹⁴ has also found negligible amounts of volatile activity in a similar procedure.

The total activity of each tissue showed a steady drop over a period of time. After 43 days the total activity was only a fraction of 1% of the original injected activity, and this was fairly evenly distributed in all the tissues examined. The individual tissues from the 43-day animal had a total activity of 0.81% of the injected dose.



The remaining carcass retained 4.73% of the original activity. Therefore 5.54% of the initial total injected dose was still present in the entire body after 43 days.

Specific activity (cpm/mg dry tissue) was also calculated for each tissue and corrected for the varying carbon content of each tissue, so as to make the values comparable. These values showed a steady drop, as can be seen in Fig. 1. Bone did not show any greater activity than any of the other tissues. (More complete and detailed data will be published in another article.)

From this data, turnover rates were calculated for each tissue and integrated into three components. If one averages the daily percent turnover of C¹⁴ of each of these three components, the estimated average components for the entire organism may be plotted on a curve from which the percent retention of injected C¹⁴ at any time may easily be seen. This is done in the curve in Fig. 2. At any one time the percent activity in the organism will be the sum of the three components.

C¹⁴ when injected into mice as methyl-labeled glycine is evenly distributed throughout the animal body. From 8% to 70% is lost as radioactive CO₂ in the breath in the first 48 hr. After this time there is a slow but steady loss in the urine, feces, and breath, so that after 43 days only 5.54% of the injected activity is present in the body, with an over-all biological half-time of 10.5 days. Turnover rates in all tissues are quite similar.

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Rate of Disappearance of Prothrombin from the Circulation¹

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The rate at which prothrombin disappears from the circulation could give important clues as to the significance and utilization of this substance in the body. The problem, however, has not received adequate attention in the literature, chiefly because of the technical difficulties met with in prothrombin determination. Warren and Rhoads (6), while investigating the formation of prothrombin by the liver, found that the prothrombin level dropped rapidly to about 20% in 10 hr and 10% in 16 hr, after total hepatectomy in dogs. Their data, unfortunately, are subject to criticism because, when the liver is removed, labile factor and prothrombin are depleted simultaneously (2); the prothrombin time expressing, therefore, the combined deficiency of both factors. Me-Ginty et al. (1), while studying the ability of purified beef prothrombin to restore the prothrombin level in dicumarolized dogs, noticed that the injected prothrombin would progressively decrease and disappear within 2 or 3 days. More analytical data were not given.

New techniques for the study of the speed of disappearance of prothrombin from the circulation have now become available with the introduction of methods for direct determination of the concentration of prothrombin (\mathcal{S}), and for simple preparation of concentrates of prothrombin (\mathcal{S}). The problem was, therefore, investigated in rabbits, in which prothrombin concentration had been drastically depressed with dicumarol treatment.

Five male rabbits of average size received daily 10 mg/kg body wt of dicumarol in gum acacia suspension,3 introduced in the stomach by intubation. After 5 days of treatment the prothrombin level of the animals was usually lower than 5% of normal, while the concentration of the labile factor, determined with the method previously described by Quick and Stefanini (4), appeared normal or slightly decreased. At this point, we injected intravenously in each rabbit a freshly prepared concentrate of prothrombin, obtained from a volume of fresh oxalated rabbit plasma equal to that of the presumed plasma volume of the animal under investigation. For working purposes, this was considered equal to 5% of the body wt of the animal. No reaction or untoward effect was noticed. The prothrombin time was then determined in plasma obtained by centrifugation at 2000 rpm for 10 min of oxalated blood collected from the central artery of the ear at various intervals after the injection (30 min, and 1, 6, 12, 24, 36, 48, 60, and 72 hr). During this phase of the experiment the rabbits continued to receive 5 mg of dicumarol per kg body wt daily to prevent any formation of prothrombin by the liver. The concentrate of prothrombin was prepared by the method of Quick and Stefanini (5), the only modification being that the final product was treated with 1/10 vol of full-strength thrombin to remove the fibrinogen still present, stored at 4° C for 1 hr, and then incubated in a water bath at 37° C for 30 min in order to inactivate any remaining thrombin. The prothrombin time was determined

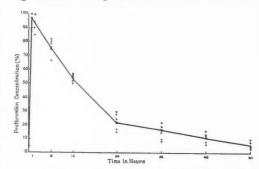


Fig. 1. The rate of disappearance of prothrombin from the circulation following intravenous injection of a concentrate of prothrombin in dicumarolized rabbits.

with the one-stage method of Quick (β) and its values were checked by determining the concentration of prothrombin directly with the technique described by Quick and Stefanini (β). The results of the two procedures usually agreed within $\pm 5\%$.

The average findings of the five experiments are presented in Fig. 1. Restoration of the prothrombin level to almost 100% of normal followed immediately the injection of the concentrate of prothrombin. About 50% of the prothrombin injected disappeared from the circulation within the first 12 hr, and about 80% in 24 hr. From this time on, a slow depletion continued until the original level was again reached, 48 hr—60 hr after the injection.

These findings show that prothrombin is promptly utilized or metabolized in the body, most of it disappearing from the circulation in the first 24 hr. The results also demonstrate that the concentrate of prothrombin prepared with the technique developed in our laboratory is capable of restoring to normal the prothrombin concentration of dicumarolized rabbits, in a definite quantitative relationship.

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¹This investigation was supported by a grant from the Division of Research Grants, National Institutes of Health.

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³ In a mortar, 250 mg of dicumarol and 5 g of finely pulverized acacia was added to 50 ml of distilled water and suspended by grinding carefully. One ml of the suspension contained, therefore, 5 mg of dicumarol. The suspension, well shaken before use, was kept in a refrigerator at 10° C.

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A New Improved Method for Determination of Prothrombin Levels in Blood¹

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A previous communication by one of the authors (1) described a simplified and accurate procedure for blood cell counts and hemoglobin determinations which had been developed for experiments on mice. Its advantages over previous methods, namely, greater precision and increased saving of time, effort, and expense, have been stressed in a recent publication in which its clinical application was described (4). It differed from similar procedures in that it used calibrated capillary tubes instead of the conventional pipettes. The use of these tubes, in addition to some technical adjustments, resulted in a reliable, practical method for the estimation of prothrombin activity.

The procedure is as follows: Capillary tubes, prepared as described previously (1), are filled with a 2% solution of potassium oxalate which is evaporated to dryness in the oven. A suspension of rabbit lung thromboplastin² is prepared according to the Link-Shapiro modification of Quick's method (2, 3), except that a stronger calcium chloride solution (0.125M), and whole blood, instead of plasma, are used. The blood is taken into tubes with dry rather than dissolved oxalate. Then 15 cu mm of the thromboplastin solution is placed on a clean glass slide.



Fig. 1. Mouse holder, 5-cu-mm capillary tube for blood samples, minute rubber bulb of the type used for smallpox vaccinations, stop watch, and glass slide on which the blood clot can be noted.

A 5-cu-mm oxalated capillary tube is filled with blood from the mouse tail (see Fig. 1). The oxalated blood

¹ This method was developed during a tenure of grants obtained by the senior author from the National Cancer Institute, U. S. Public Health Service, and from the Damon Runyon Fund.

²A satisfactory commercial preparation is made by the Maltine Co.

is quickly pressed out into the thromboplastin on the glass slide with the aid of a minute rubber bulb, of the type used for smallpox vaccinations (Fig. 1), and the blood and thromboplastin are mixed gently. The stop watch is started at the same instant that the blood is added to the thromboplastin. The mixture on the glass slide is drawn in and out of the capillary tube by gently pressing the rubber bulb, avoiding air bubbles. At each filling, the capillary tube is lifted up slightly to permit observation of the formation of the fibrin strand. The latter can be noticed suddenly, giving a clearly defined end point of blood clotting. When it appears, the stop watch is instantly stopped and the time is noted. Table 1 summarizes the results obtained by the use of this method on normal Swiss white mice.

TABLE 1
PROTHROMBIN LEVELS OF WHITE MICE, SWISS STRAIN

No. of	Deter-	Temp.	Prothrombin time in sec:		_		
	mina- tions		lowest	highest	mean	Devi- ation	Remarks
40	40	23	19	31	28.4	2.7	Single deter- minations
9	20	26.5	20	32	24.9	2.5	Repeated de- terminations
7	18	28.5	18	24	22.9	3.7	within 3 days, at 24-hr in- tervals

The method has proved to be simple, reproducible, and economical. A major advantage is that the test can be performed promptly and with small volumes (5 cu mm) of blood, thus avoiding the necessity for venipuncture. In small species, such as mice, it permits repeated determinations on the same animal with only negligible trauma to the tip of the mouse tail and loss of only insignificant volumes of blood. In man, the method permits the bedside determination of prothrombin time from blood obtained by finger puncture. However, the method introduces two new variables which warrant consideration. 1) Since the method uses whole blood, subjects with low hematocrit values may have greater plasma volumes per aliquot of whole blood. 2) The test is performed at room temperature rather than in a constant temperature water bath. These factors may cause small but significant variations, which may be corrected or taken into account in problems calling for greater accuracy. The relatively narrow range of average deviation indicates that the technique is sensitive and reliable.

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- 2. QUICK, A. J. Proc. Soc. exp. Biol. Med., 1939, 42, 788.
- Shapiro, S. et al. Proc. Soc. exp. Med. Surg., 1942, 50, 85.
- WROBLEWSKI, F., WEINER, M., and SHAPIRO, S. J. clin. Path., 1949, 2, 138.

Comments and Communications

Chemistry in Postwar Europe

As a result of the trip that one of my associates and I took to France, Switzerland, Germany, Holland, Denmark, Sweden, and England in the late spring and early summer of 1948 and, as a result of conversations with people in this country since our return, we have the impression that American chemists do not fully appreciate the amount of fine work that is being carried on in Europe today and the amount that was done even during the difficult years of the war when Europeans carried on research in the pure sciences and also in the field of the applied sciences aside from those of military import.

In Switzerland, some outstanding work on the partial synthesis of several adrenal hormones was carried on in Basel in the laboratories of Thadeus Reichstein. Dr. Reichstein was born in Poland a little over 50 years ago. He was a student of the German chemist, Staudinger. For a time he was on the faculty of the Technische Hochschule in Zurich and is well known on this side of the Atlantic as a result of several visits to the U. S. Some excellent work on the steroids was carried on in his laboratory during the war. Those who are working in this field in the U.S. were particularly interested in his synthesis of dehydrocorticosterone in 1943. He also has done some very interesting work on the synthesis of glycosides, part of which was done in collaboration with his distinguished fellow countryman, D. L. Ruzicka, head of the Chemical Institute of the Technische

Prof. Ruzicka was born in Yugoslavia. He, too, was a student of Staudinger. He is particularly well known for research on the chemistry of perfumes, such as musk, and has also done much work on organic compounds with large ring structures. His laboratory is well equipped and staffed. During the war he investigated the relationship between odor and chemical constitution and the constitution of iris root principles.

Hochschule in Zurich.

In France, some exceptional work in the field of antihistaminic and and antiallergic drugs resulted in the development of valuable antihistaminic products.

We visited several French chemists, among them M. E. Fourneau, under whom the writer had carried on research in the Institut Pasteur more than 20 years ago. M. Fourneau, in his late 70's last year, was still actively carrying on and directing research work. It was he who first synthesized the local anesthetic stovaine, and who developed one of the useful arsenicals, stovarsol, for the treatment of syphilis and amebic dysentery. He and his co-workers also determined the structure of the German secret medicinal agent Bayer 205, which was greatly publicized as an agent for the treatment of sleeping sickness in the years immediately after the first World War. It was in his laboratories that the value of sulfanilamide for the treatment of bacterial infections was first determined.

M. Fourneau carried on research during the war in the field of synthetic medicinals. Among other things, he did

some interesting work on choline compounds and on their remarkable blood pressure-lowering effects. Immediately after the war, amid the confusion and misunderstandings which followed the German occupation, he spent a few months in a French prison. Happily, before his recent death, he was able to resume work in a fine new laboratory with 10 or 12 scientific assistants made available to him by one of the large chemical manufacturing companies of France.

In Paris, some of the laboratories are not so modern as one finds in the better institutions in this country and in some places in Europe, but the laboratories in the relatively new Ecole Normale Supérieure are excellent. Fine research work is being carried out here under the direction of Profs. Vavon and DuPont. Also, fine research is in progress in the laboratories of the leading chemical and pharmaceutical concerns of France.

In Germany, conditions for scientific work since the war have not been at all good. The best laboratories are probably those maintained in the large scientific institutes of the big industries. The writer was particularly impressed by the research on synthetic antitubercular agents going on in Prof. Domagk's laboratory in the former I. G. plant at Elberfeld. The laboratories of the former I. G. plant at Hoechst, too, seemed well equipped.

There are also a few academic and institutional laboratories carrying on interesting investigations in Germany, for example, that of E. R. Kuhn, head of the Kaiser-Wilhelm Institute in Heidelberg. He is well known for his work on the structure and synthesis of natural products, such as riboflavin and the synthesis of vitamin B₆. During the war he carried on research on antivitamins and some very interesting work on the effect of chemicals on the sex characteristics of cells.

In Göttingen, an interesting new development was begun in 1947 by the joint American-British Military governments. It is a new scientific institution known as the Max Planck Institute for Scientific Research, with head-quarters in the former German Air Force laboratories, which were about to be destroyed by the British forces when the scientific representative of the British Military Government heard of it. He was able to prevent this destruction and, in cooperation with an American colleague carrying on similar work for the American government, succeeded in turning these laboratories into a place for peaceful scientific work by leading German scientists in Western Germany.

The institute is headed by O. Hahn, who was formerly head of the Chemical Laboratory of the Kaiser-Wilhelm Institute in Berlin. The central laboratories are in Göttingen, but a number of other Max Planck Institutes are being, or have been, established in other parts of Germany, replacing those which were formerly known as Kaiser-Wilhelm Institutes. A concise account of scientific investigations in biology, chemistry, mathematics, physics, medicine, and earth sciences during the period

from May 1939 to May 1946, has recently appeared in the Fiat Review of German Science.

One encounters more serious shortages in Germany than anywhere else in so-called Western Europe. In the first place, many of the scientific libraries were destroyed. In those still intact, there are practically no publications dating from any time since the beginning of World War II except those published in Germany. There is comparatively little equipment left in the laboratories, and there is a great shortage of the chemicals required in laboratory study and research.

From Germany, during the war, came some interesting new analgesic drugs, some of which have narcotic action similar to that of morphine. One of these, known as methadone in this country, is being used as a narcotic and as a substitute for morphine. Both in Germany and in Sweden new blood substitutes were found which have proved useful: periston, which was developed in Germany, and dextran, in Sweden.

The main impression gathered in the Scandinavian countries was the excellence of the biochemical work, particularly that in the field of enzymes, being done in the laboratories of such outstanding investigators as Linderstrom-Lang, Kalekar, Theorell, and Tiselius. This work was all made possible by use of some of the most modern physical and physicochemical techniques.

In Sweden, a valuable new synthetic local anesthetic known as xylocaine was developed during the war years. We understand it will be introduced into use in this country shortly.

Some interesting work in organic chemistry is being done in the Royal Institute of Technology in Stockholm. The laboratories are well planned and well equipped. The head of the Department of Organic Chemistry is H. Erdtman, a one-time student of Sir Robert Robinson in England. He is doing some brilliant work on the structure of the chemical constituents of wood. He has recently found, for example, a number of products present in the heartwood of various trees which prevent its ready decay.

From wartime England came two significant developments in the field of medicinal chemistry. The most outstanding, of course, was penicillin. The second was the discovery of an entirely new type of antimalarial, known as paludrine.

At present there are a number of famous laboratories where work is going on at full pace. This work may be judged as most outstanding by any standard. First mention will be made of the laboratories of Sir Robert Robinson, president of the Royal Society of Great Britain. Lady Robinson also is a chemist. Sir Robert paid a number of visits to the U. S. during the war years. Those of us who came in contact with him during that time grew to appreciate more than ever the vigorous clarity of his thinking and the originality of his approach to research problems. Sir Robert is well known for his work on the coloring matter of plants, the chemistry of penicillin, the structure of strychnine, the structure and syn-

thesis of steroids, and studies in a number of other important fields. He has a large staff of competent men working with him.

Some of the leading scientists visited in England were R. A. Peters, head of biochemistry at Oxford University, Sir Ian Heilbron, head of the Department of Chemistry in Imperial College, and A. R. Todd, head of the Department of Chemistry, Cambridge University.

Prof. Todd is one of the younger scientific leaders in England today. He was born in Scotland and studied under Barger and others at Edinburgh. He was temporarily on the faculty of the California Institute of Technology, but shortly before the war he accepted the position of head of the Chemistry Department at the University of Manchester. He left his post during the later war years to become head of the Department of Chemistry at the University of Cambridge. Prof. Todd has done considerable work on the synthesis of vitamin B₁ and on the chemistry of Cannabis indica. Recently he has investigated the structure and synthesis of nucleosides and nucleotides, including a classic synthesis of adenosine triphosphate, which was published recently in The Journal of the Chemical Society of Great Britain.

We were delighted to learn the extent to which British chemical industry feels that it should depend upon scientific research for its future growth. For example, in Manchester we were shown plans for a great new pharmaceutical laboratory to be built for research in the pharmaceutical and medicinal chemical field.

As a result of the disruptions occasioned by the war, many of the scientific libraries in Europe do not contain recent publications from other parts of the world. Some of them contain little, if anything, beyond 1939–1940. Also, it is unfortunately true that many American scientific libraries have been unable to obtain scientific publications that appeared in Europe during and since the war.

One of our friends recently prepared a bibliography of all publications obtainable in this country on the medical properties of one of the newer antibiotics. While in Switzerland, he learned that a bibliography on this new antibiotic had just appeared there. Much to his astonishment, he found that there was comparatively little duplication of references in the two bibliographies. The bibliography prepared in this country contained American references largely, and the bibliography published in Europe consisted chiefly of European references.

The gaps in the files of America's scientific libraries would have been still greater if Switzerland had not acted for some time as a channel for the supply of European journals abroad. The system by which the U. S. Office of Alien Property Custodian, in the public interest, reprinted and distributed German scientific journals was also helpful. No such system seems to have prevailed in Europe, and hence their files are quite barren of wartime foreign journals.

RANDOLPH T. MAJOR

Merck & Co., Inc., Rahway, New Jersey

Book Reviews

World of Life: A General Biology. Wolfgang F. Pauli. Boston 7: Houghton Mifflin, 1949, 653 pp. \$5.00.

Wolfgang Pauli's new book The World of Life is designed to be a main reading source for a general biology course. As such it is quite original in its organization, being based on the view that a textbook benefits as much from an underlying thesis or a general principle to be expounded as does any other type of book. Usually we find in a biology textbook no continuous flow of ideas and no fundamental pattern except for whatever organization the subject matter may itself possess, so that we are accustomed to such chapter headings as "Protozoa," "Coelenterates," "Flatworms," "Mollusks," and "Arthropods." Thus, the average textbook tends to be a compendium of data, observations, and hypotheses, and it leaves synthesis and organization to the student reader who, we may guess, will be so lost in the welter of detail as to lose sight of the forest for the trees. Happily, The World of Life does not share this tendency with the average textbook with which we are familiar.

The thesis of Dr. Pauli's book is the evolution of living things. After setting the stage with Parts One and Two ("Backgrounds: The Physical World," and "The Nature of Life"), the author discusses the principle of evolution in Part Three, and gives an evolutionary treatment of the plants in Part Four, and a similar treatment of the invertebrates and vertebrates in Parts Five and Six. In Part Seven he discusses the physical basis of heredity (the "raw materials of evolution") and the implications genetics has for human survival and evolution. Woven into this pattern are the structural and functional aspects of the parts of the many organisms described in the book.

The World of Life has several unfortunate aspects. Dr. Pauli, assuming that his general biology student may have no knowledge of chemistry and physics, tries to make up for this deficiency by offering an elementary review of general physics and chemistry in a futile section of eighteen pages. Consequently, he is forced to omit from consideration many important biological problems whose formulation and study require a more solid grasp of modern physical and chemical principles and data. Among the fundamental problems that are either treated inadequately or left out of the book are: autocatalysis; differentiation, growth and morphogenesis in terms of chemical changes; the relation between genes and metabolic processes; the physicochemical nature of mutations; the integration and coordination of metabolic events. Yet discussions of these problems and the ways in which they are being attacked certainly belong in a college student's main reading source in biology.

Another serious defect of the book is its failure to instruct in the scientific method. It has the style of a "Book of Knowledge," too often asserting and presenting the final story without indicating how such a story was developed. Opportunities are sadly missed to dem-

onstrate the weeding-out of alternative hypotheses that explain given phenomena, and to differentiate between hypotheses that are meaningful and those that are not. Indicating how modern biologists have arrived at their concepts would have made a wonderful lesson in the methods and aims of science.

The student reader will also have to be guarded against such incautious and hasty generalizations as: "It seems quite clear that particular genes determine the presence of the specific enzymes essential for the individual chemical steps of metabolic processes" (italies mine); and again, in a caption to a figure showing various types of specialized cells in a multicellular organism: "Each [of these cells] has the same kind of chromosomes, and hence the same genic components."

What are serious faults in a book for a college course, making it probably unsuitable for use there, may be negligible in a book for senior high school or junior college students. For them, the highly readable style, the attractive instructive format, and the illustrative material may well make up for such defects.

ARNOLD W. RAVIN

Columbia University

Scientific Book Register

Research in Medical Science. David E. Green and W. Eugene Knox, Eds. New York: Macmillan, 1950. 492 pp. \$6.50.

The Chemistry of Heterocyclic Compounds: The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, Bismuth, and Silicon. Frederick George Mann. New York-London: Interscience, 1950. 180 pp. \$5.25.

Science Is a Sacred Cow. Anthony Standen. New York: E. P. Dutton, 1950. 221 pp. \$2.75.

Advances in Electronics, Vol. II. L. Marton, Ed. New York: Academic Press, 1950. 378 pp. \$7.60.

La Biologie des Lépidoptères. P. Portier. Encyclopédie Entomologique, Vol. XXIII. Paris VIº: Paul Lechevalier, 1949. 643 pp.

Coagulation, Thrombosis, and Dicumarol: With an Appendix on Related Laboratory Procedures. Shepard Shapiro and Murray Weiner. New York 25: Brooklyn Medical Press, 1949. 131 pp. \$5.50.

Hematin Compounds and Bile Pigments: Their Constitution, Metabolism, and Function. R. Lemberg and J. W. Legge. New York: Interscience, 1949. 745 pp. \$15.00.

The Emotional Life of the Ill and Injured: The Psychology and Mental Hygiene of Rehabilitation and Guidance. Arthur Jess Wilson. New York 23: Social Sciences Publs., 1950. 416 pp. \$4.75.

Third Symposium on Combustion and Flame Explosion Phenomena. Baltimore: Williams & Wilkins, 1949. 748 pp. \$13.50.

NEWS and Notes

Maurice Goldhaber, professor of physics at the University of Illinois, has been appointed to the Department of Physics at Brookhaven National Laboratory where he will direct studies of the energy levels of atomic nuclei. Dr. Goldhaber's wife, Gertrude Scharff-Goldhaber, will also join the Brookhaven staff. Her research has been with neutrons, photoneutrons, and nuclear disintegration.

Maurice I. Smith, chief pharmacologist in the U. S. Public Health Service, is retiring after 30 years of research at the National Institutes of Health and the Hygienic Laboratory, its predecessor. His work there has included studies on the assay of pituitary extracts, on B complex vitamins, on DDT and other insecticides, and on the chemotherapy of tuberculosis.

Lewis K. Sweet has been appointed chief of the newly established Clinical Unit of the Microbiological Institute, National Institutes of Health. Dr. Sweet has been chief medical officer at Gallinger Municipal Hospital in Washington, D. C., since 1938.

Royal Merrill Frye, formerly of Boston University, has been appointed professor of physics at Simmons College, Boston. Dr. Frye's special field is spectroscopy, and he was in charge of gathering spectrographic data at the Bikini atom bomb tests in 1946.

John Salem Lockwood, professor of surgery at Columbia University, has been appointed clinical director and chief of surgical services at Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City, to take charge July 1. Allen O. Whipple, present director of clinical activities, will give his full time to supervising educational work at the Memorial-Cancer Center.

Otto A. Reinking will retire April 30 as professor of plant pathology and head of the division at New York State Agricultural-Experiment Station, Cornell University. He has accepted an appointment as an agriculturist with the U. S. Department of Agriculture, Office of Foreign Agricultural Relations, and has been assigned as counselor in plant industry and plant pathology to the Philippine Government in Manila.

Visitors to U. S.

Ronald A. Fisher, statistician of the University of Cambridge, England, recently lectured at the Michelson Laboratory, Naval Ordnance Test Station, Inyokern, California.

Niels Bohr, physicist at the University of Copenhagen, and J. T. Henderson, chief of the Electricity Section, National Research Council of Canada, Ottawa, were recent visiters at the National Bureau of Standards.

S. L. Tandon, lecturer in botany at the University of Delhi, has been appointed research assistant in botany at the State College of Washington, Pullman, Washington.

Grants and Awards

A \$52,500 Rockefeller Foundation grant has been given the University of Michigan's Research Center for Group Dynamies. Work to be done under the grant will be in developing methods for measuring factors that hold groups of persons together and studying the way ideas and information circulate within a group.

Recipients of the \$1,000 Borden Awards for 1949 have been announced by the professional and scientific organizations administering the awards, as follows: Association of American Medical Colleges—Fuller Albright, associate professor of medicine, Harvard Medical School, and physician, Massachusetts General Hospital, for his work on the metabolism of bone and other tissues rand their relation to the renal and rendocrine factors that control them;

American Veterinary Medical Assoeiation-Raymond R. Birch, professor emeritus of veterinary research, New York State Veterinary College, Cornell University, for research on brucellosis; American Home Economics . Association-Kate Daum, head of the Department of Nutrition, University Hospitals, and associate professor of dieteties, Department of Internal Medicine, College of Medicine, State University of Iowa, for studies on the iron metabolism of normal women: American Institute of Nutrition-Harry J. Deuel, Jr., dean of the Graduate School, University of Southern California, for work on vitamin A and the nutritional value of fats; American Dairy Science Association-Francis J. Doan, professor of dairy manufacturing, Pennsylvania State College and Agricultural Experiment Station, for various researches on milk; Poultry Science Association - Richard M. Fraps, physiologist, Bureau of Animal Industry, Department of Agriculture, for research on the physiology of avian reproduction; American Chemical Society-George R. Greenbank, research chemist, Bureau of Dairy Industry, Department of Agriculture, for various studies on milk and milk products; American Academy of Pediatries-Alfred H. Washburn, director, Child Research Couneil of Denver, and professor of pediatrics and chief of the Department for the Study of Human Growth, University of Colorado, for work on blood diseases in children, and human growth and adaptation; Ameriean Dairy Science Association-George H. Wise, head of animal nutrition, Department of Animal Industry, North Carolina State College, for work on forages and the physiology of dairy calf nutrition.

A Frederick Gardner Cottrell grant of \$5,000 has been awarded by the Research Corporation to Stephen S. Friedland, of the University of Connecticut, for investigation of the mechanism of Geiger discharge by means of mass spectrometer studies.

The 1950 \$1,000 award of the American Urological Association for research on the male reproductive tract will be present to Carl R. Moore, chairman of the Department of Zoology, University of Chicago, at the association's annual meeting in Washington, D. C., May 29.

Fellowships and Prizes

The University of Massachusetts, through the Lotta Crabtree Foundation, is offering two graduate fellowships in the field of agriculture. The fellowships, available annually, carry a stipend of \$2,000 and cover tuition. They are open to qualified students working for the doctorate degree in some recognized phase of agriculture. Further information may be obtained from F. J. Sievers, director of the Graduate School, University of Massachusetts, Amherst.

The National Paraplegia Foundation announces the establishment of a limited number of fellowships for research in spinal cord disease and trauma and in their associated complications. These fellowships carry a minimum stipend of \$3,000 per year and are open to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious The fellowships will be awarded by the Medical Advisory Committee during the academic year 1950-51. Application forms may be obtained from L. W. Freeman, Chairman, Medical Advisory Committee, National Paraplegia Foundation, Hotel La Salle, Chicago 2, and should be submitted not later than June 1.

The fifth annual AAAS-George Westinghouse science writing competition for two awards of \$1,000 each has been announced. One award will be made for the outstanding science news story published in 1950 by a newspaper or press association. The other award will go to the writer of the best article on science published during the year in a nontechnical magazine. Entries will be judged on initiative. originality, scientific accuracy, and clarity of interpretation, and for their value in promoting a better understanding of science by the public.

The board of judges, representing

science, the public, and the news and magazine writing crafts, will be announced later. The awards will be presented next December 28 in Cleveland, Ohio, at the annual meeting of the AAAS, which administers the science writing competition.

In the newspaper competition, entries submitted must have been published between October 1, 1949, and September 30, 1950; in the magazine field, entries must have been published in issues dated between October, 1949, and September, 1950, inclusive. All entries must be posted before midnight, October &.

The rules governing the newspaper competition require each entrant to submit three separate articles published during the contest year and to designate one of the three as the entry upon which he wishes to be judged. All three may have been published by the same newspaper or carried by the same press association.

Entry blanks with detailed rules for the 1950 AAAS-George Westinghouse science writing awards may be secured from Howard A. Meyerhoff, Chairman, Managing Committee, 1515 Massachusetts Avenue, N.W., Washington 5, D. C.

The 1949 newspaper award went to Lester Grant of the New York Herald Tribune for his series on cancer, and the magazine award was presented to George W. Gray, a freelance writer, for his article on the human brain, "The Great Ravelled Knot," which appeared in the Scientific American.

The awards are made possible by a grant from the Westinghouse Education Foundation.

The Iowa State University College of Medicine is offering two fellowships in medicine to graduates of approved medical schools, on the basis of half-time teaching and half-time research in the Departments of Anatomy, Bacteriology, Biochemistry, Pathology, Pharmacology, Physiology, and Hygiene and Public Health, including Parasitology. Candidates need not have had clinical internships. The salary will be \$3,600 on a 12-month basis for single candidates, and \$4,000 for married candidates. Applications should be sub-

mitted by May 1 to the Office of the Dean, College of Medicine, State University of Iowa, Iowa City, Iowa.

Summer Programs

A vertebrate zoology field course, conducted by W. Frank Blair, will be offered by the Department of Zoology, University of Texas, June 7 to July 15, in the northwestern part of the Texas Panhandle. Work will include ecological surveys, collection and identification of vertebrate specimens, and application of methods of measuring vertebrate home ranges and population densities. Independent effort is encouraged, and students may work on problems of their own choice within the scope of the course. A major project will be the study of possible routes of vertebrate dispersal across the high plains. The course is open to male advanced undergraduate and graduate students in the biological sciences. Enrollment in the first semester of the university summer session and payment of a special field course fee of \$40 are required. Further information may be obtained from W. Frank Blair, University of Texas, Austin.

The Fish and Wildlife Service of the Department of the Interior announces that laboratory space will again be available for summer researchers at its Beaufort Station in North Carolina. Guest investigators will be furnished with large individual research bays in which to work, a skiff for local collecting, and sleeping accommodations. The station has aquaria tanks and fresh and salt water ponds. Facilities for radioisotope studies on nutrition or other physiological problems of invertebrates will be available to qualified investigators.

Applicants will be chosen on the basis of education, research experience, and applicability of their research to fishery or related marine problems. The service is especially interested in having two investigators who will work on the physiology of the shad (Alosa sapidissima). Applications and information may be obtained from Clinton E. Atkinson, Chief, Middle and South Atlantic Fishery Investigations, Fish and

Wildlife Service, Beaufort, North Carolina. Applications must be returned to the station by May 15, when a total of eight investigators will be chosen.

Industrial Laboratories

David R. Schwarz, of Schwarz Laboratories, Inc., New York City, left last month to spend six weeks in England, France, Belgium, Italy, and Switzerland, where he will study the increasing demand in Europe for some of the rare chemicals and pharproduced maceuticals now Schwarz Laboratories, Inc. through its Fine Chemicals Division. Of special interest among these compounds are such fermentation intermediates as adenosine triphosphate, the phosphorylated sugars, and coenzyme I.

The Bjorksten Research Laboratories, specializing in technical development work for industry, have established an office in New York City, at 50 East 41st Street. The Chicago office of the laboratories will continue operations under the direction of Edwin L. Gustus, vice president. Johan Bjorksten, president, will divide his time between the New York office and the research laboratories of the corporation in Madison, Wisconsin.

The Sterling-Winthrop Research Institute of Rensselaer, New York, is completing a new group of laboratories, including an underground unit, for research in organic chemistry at various pressures. Other laboratories and the administrative center are completed and in operation. The new Chemical Development Laboratory will be officially dedicated May 17–18. It is to be under the direction of B. F. Tullar and E. D. Homiller.

Meetings and Elections

A symposium on the basic aspects of radiation effects on living systems will be held at Oberlin College June 14–18. It was arranged by the Committee on Radiobiology of the National Research Council, and is intended to provide a thorough

survey of radiation effects through five panel discussions of the contributing fields of research.

The sessions and panel speakers are: "The Physical Processes Involved in the Interaction of Radiation and Matter"-H. M. Parker, R. D. Evans, Ugo Fano, C. A. Tobias, R. R. Wilson; "The Chemical Changes Resulting from the Absorption of Radiation''-James Franck, Milton Burton, Henry Eyring, Robert Livingston, R. L. Platzmann; "The Biochemical Processes Resulting from the Interaction of Radiation and Biological Tissues''-E. S. G. Barron, W. M. Dale, Georg Hevesy, M. D. Kamen, Raymond Latarjet; "Cellular Changes and Effects Produced by Radiation''-R. E. Zirkle, N. H. Giles, Alexander Hollaender, H. J. Muller; and "Effects of Radiation on the Whole Mammalian Organism''-A. M. Brues, D. R. Charles, T. C. Evans, H. B. Jones, and Shields Warren. Those interested in attending the symposium should write to Dr. Harvey M. Patt, Argonne National Laboratory, P. O. Box 5207, Chicago 80 (not later than April 15).

A symposium on application of spectroscopy in the petroleum industry will be held May 16 at Armour Research Foundation of Illinois Institute of Technology, under the sponsorship of the Chicago Chapter of the American Association of Spectrographers.

The 31st annual session of the American College of Physicians will be held in Boston, April 17-21. Headquarters will be the Mechanics Building, 111 Huntington Avenue, where general sessions and panel discussions will be held and the technical exhibit will be located. A new feature in the program will be color television clinies, in addition to the regular hospital clinics.

A symposium on general cytology will be held May 1-2, under the sponsorship of the Departments of Bacteriology, Biological Science, Botany, Physiology, and Zoology at Michigan State College. The four speakers on the program are Franz Schrader, Columbia University, C. Leonard Huskins and Hans Ris, Uni-

versity of Wisconsin, and William Doyle, University of Chicago. Further information can be obtained from Ralph W. Lewis, Department of Biological Science, Michigan State College, East Lansing.

The first meeting of the newly organized Histochemical Society was held at the University of Pennsylvania Medical School in Philadelphia March 24-25 and the following officers were elected: president, G. B. Wislocki, Harvard University; vice president, D. Glick, University of Minnesota; secretary, R. D. Lillie, National Institutes of Health; and treasurer, E. W. Dempsey, Harvard University.

The National Science Foundation Bill. On March 27 the Senate formally requested a conference with the House of Representatives to resolve the differences between the Senate and House National Science Foundation bills. Senate members of the conference committee are: Elbert D. Thomas, James E. Murray, Herbert H. Lehman, Robert A. Taft, and H. Alexander Smith. House conferees are J. Percy Priest, Andrew J. Biemiller, George H. Wilson, Carl Hinshaw, and Joseph P. O'Hara.

The following letter to Senator E. D. Thomas from Roger Adams, AAAS president, dated March 14, states the opinion of the Association on the loyalty amendment to the bill, introduced by Representative Howard W. Smith:

The scientists of the American Association for the Advancement of Science, nearly forty-five thousand in number, have been essentially unanimous in support of the National Science Foundation Bill. We have noted, however that a very unfortunate amendment was attached to the Bill which reads as follows:

No person shall be employed by the Foundation and no scholarship shall be awarded to any person by the Foundation unless and until the Federal Bureau of Investigation shall have investigated such person and reported to the Foundation that such person is loyal to the United States, believes in our system of government and is not and has not been at any time a member of any organization declared subversive by the Attorney General or any organization that teaches or advocates the overthrow of the government by force or violence.

Speaking for the Association, I urge you to do everything possible to eliminate this amendment. You realize that the Atomic Energy Commission has funds for the support of scientific men who are working in the atomic energy field where secret information is involved. They must be and should be cleared by the Federal Bureau of Investigation. The students who will benefit by the National Science Foundation Bill will not be working in research of a secret character and, therefore, should not be required to submit to an FBI investigation. The amendment is worded so that any individual who might have been attached at any time to any organization which is now considered subversive by the Attorney General would be excluded from help under the National Science Foundation Bill. This is particularly objectionable since many organizations now considered subversive were not considered so until recently. The amendment provides that the Federal Bureau of Investigation has the final word and the individual is not permitted to defend himself against unjust decisions. This amendment is even more rigid than that required of those who will have access to secret information.

I trust that you will understand the point of view of the scientists in asking you to have this amendment eliminated. They are as interested as the congressmen in protecting the United States against those who advocate overthrow of our present government. They are opposed, however, to unnecessary procedures which inevitably will delay appointments of competent scientists for research work and to regulations which do not permit accusations to be open and publicized. The National Science Foundation should be given the authority of scrutinizing carefully the individuals who are appointed and if there is any doubt in their minds concerning the loyalty of the individuals the matter could be referred to the Federal Bureau of Investigation.

Two new AAAS volumes will be published next month: Centennial, a collection of papers presented at the AAAS Centennial Celebration held in Washington, D. C., September 13–17, 1948, and Brucellosis, papers read at the symposium sponsored last September by the National Institutes of Health, the National Research Council, and the Department of Agriculture.

Most of the symposium volumes published by the AAAS have been based upon special programs of its sections, its affiliated societies, and its Gordon Research conferences. In publishing the papers presented at the brucellosis symposium, the association is extending its publishing interests to activities sponsored by other scentific organizations, thus furthering its objective of increasing public understanding of the work of scientists and their progress in specific fields.

Members' advance order prices are: Centennial (about 320 pages) \$3.75; Brucellosis (about 308 pages) \$2.75. Checks or money orders may be mailed to AAAS Publication, 1515 Massachusetts Avenue, N.W., Washington 5, D. C.

The Office of Naval Research Biological Sciences Division and the Atomic Energy Commission Division of Biology and Medicine have agreed to administer separately their former joint program of financial support for research projects conducted by universities and other research institutions. Most of the projects concerned will continue to receive financial support from the AEC, and Navy-owned equipment will be maintained on loan at those institutions where continued interest exists. The decision, made at a recent conference of the two divisions, will enable the AEC to establish a closer working relationship with seientists in its field of interest, and will make it possible for the ONR to assist other areas of the biological seiences not as amply supported at present.

A program for the eradication of yaws and syphilis in rural areas of the Latin American regions has been set up by the Pan American Sanitary Bureau, regional office of the World Health Organization, in collaboration with the UN International Children's Emergency Fund. Sacha Levitan, consultant on venereal disease, and Adhemar Paoliello, an expert in mass treatment of populations, are now in Haiti making a survey of available facilities, and will assist in the operation of the project. The program for total elimination of these diseases will be carried out through mass procedures for diagnosis and treatment, establishment of permanent treatment dispensaries and mobile units, and organization of a system of case finding through home visits. It is planned to extend the campaign to the Dominican Republic soon.

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The PASB is also sending Federico Gomez, consultant in maternal and child health, on a four-month trip through Latin America to gather information for a health-program to reduce infant mortality in those countries.

The Museum of Zoology of the University of Michigan has received a collection of study skins of birds of Canada and the U. S., collected by the late Max M. Peet. The collection of 30,000 specimens includes examples of many rare or extinct species—for example, the only two known specimens of Sutton's Warbler.

Make Plans for-

Association of Southeastern Biologists, annual meeting, April 7-8, University of Virginia, Charlottesville, Virginia.

American Association of Pathologists and Bacteriologists, annual meeting, April 14-15, Madison, Wisconsin.

American College of Physicians and Surgeons, annual meeting, April 17-21, Boston, Massachusetts.

Federation of American Societies for Experimental Biology, annual meeting, April 17–21, Atlantic City, New Jersey.

Electrochemical Society, annual meeting, April 19-22, Hotel Statler, Cleveland, Ohio.

Third World Health Assembly, opening, May 8, Geneva, Switzerland.

International Symposium on Use of Chloramphenicol, June 3-5, Milan, Italy.

Nutrition Conference, UN Food and Agriculture Organization, June 5-15, Rio de Janeiro, Brazil.

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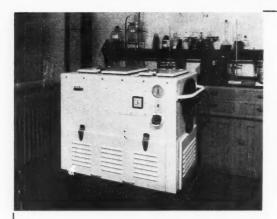
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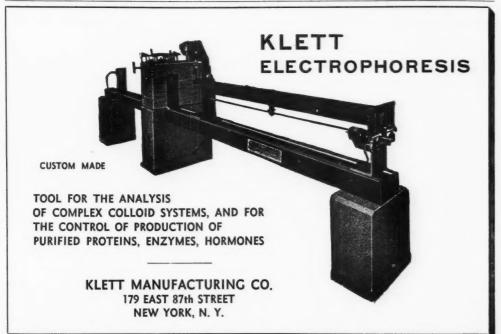
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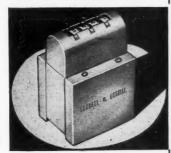
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